

We claim:

1. A method of identifying a polynucleotide of a microbe that is expressed *in vivo* comprising the steps of:
 - (a) adsorbing antibodies against antigens that are expressed by the microbe *in vivo* and *in vitro* with cells or cellular extracts of the microbe that have been grown *in vitro*;
 - (b) isolating unadsorbed antibodies; and
 - (c) probing an expression library of the microbe's DNA or RNA with the antibodies of step (b);
- 10 wherein a polynucleotide of the microbe that is expressed *in vivo* is isolated and identified.
2. The method of claim 1 wherein the polynucleotide encodes an antigen.
3. The method of claim 2 wherein the antigen is capable of eliciting an immune response in an animal.
- 15 4. The method of claim 3 wherein the animal is selected from the group consisting of humans, baboons, chimpanzees, macaques, cattle, sheep, pigs, horses, goats, dogs, cats, rabbits, guinea pigs, rats, mice, chickens, ducks, fish, and shellfish.
5. The method of claim 1 further comprising the step of determining the nucleic acid sequence of the polynucleotide.
- 20 6. A method of confirming the identified polynucleotide of claim 1 as expressed *in vivo* comprising the steps of:
 - (a) expressing and isolating a polypeptide from the identified polynucleotide of claim 1;

(b) producing antibodies to the polypeptide; and

(c) probing biological samples from a host infected with or previously infected with the microbe, with the antibodies of step (b),

whereby the identified polynucleotide is confirmed as being expressed *in vivo*.

- 5 7. The method of claim 1 wherein the antibodies of step (a) comprise sera from one or more hosts infected with, or previously infected with the microbe.
8. The method of claim 1 wherein the microbe is selected from the group consisting of a bacterium, a virus, a parasite, a prion, and a fungus.
9. The method of claim 1 wherein the microbe is selected from the group consisting
- 10 of *Candida*, *Aspergillus*, *Sporothrix*, *Blastomyces*, *Histoplasma*, *Cryptococcus*, *Pneumocystis*, *Coccidioides*, *Tinea*, *Toxoplasma*, *Plasmodium*, *Pseudomonas*, *Actinobacillus*, *Staphylococcus*, *Bacillus*, *Clostridium*, *Listeria*, *Corynebacterium*, *Actinomyces*, *Mycoplasma*, *Nocardia*, *Bordetella*, *Brucella*, *Francisella*, *Legionella*, *Enterobacter*, *Escherichia*, *Klebsiella*, *Proteus*, *Salmonella*, *Shigella*, *Streptococcus*,
- 15 *Yersinia*, *Vibrio*, *Campylobacter*, *Helicobacter*, *Bacteroides*, *Chlamydia*, *Borrelia*, *Treponema*, *Leptospira*, *Aeromonas*, *Rickettsia*, *Ascaris*, *Cryptosporidium*, *Cyclospora*, *Entamoeba*, *Giardia*, *Shistosoma*, *Trypanosoma*, herpes virus, cytomegalovirus, Epstein-Barr virus, hepatitis virus, adenovirus, papillomavirus, polyomavirus, enterovirus, rotavirus, influenza virus, paramyxovirus, rubeola virus,
- 20 rhabdovirus, human immunodeficiency virus, arenavirus, rhinovirus, and reovirus.
10. The method of claim 1 wherein the host is an animal selected from the group consisting of comprise humans, baboons, chimpanzees, macaques, cattle, sheep, pigs,

horses, goats, dogs, cats, rabbits, guinea pigs, rats, mice, chickens, ducks, fish, and shellfish.

11. A method of comparing polynucleotides of a microbe that are expressed *in vivo* at different stages of infection of the microbe comprising the steps of:

- 5 (a) adsorbing a first sera sample from one or more hosts infected with or previously infected with the microbe, with cells or cellular extracts of the microbe that have been grown *in vitro*, wherein each host is in about the same stage of the infection;
- (b) adsorbing a second sera sample from one or more hosts infected with or previously infected with the microbe, with cells or cellular extracts of the microbe
10 that have been grown *in vitro*, wherein each host is in about the same stage of the infection, wherein the stage of the infection is different from the stage of infection in step (a);
- (c) isolating unadsorbed antibodies from the first serum sample and from the second serum sample;
- 15 (d) probing a first expression library of the microbe with the unadsorbed antibodies from the first serum sample, and probing a second expression library with the unadsorbed antibodies from the second serum sample, wherein polynucleotides of the microbe that are expressed *in vivo* are identified for the first and second serum sample; and
- 20 (e) comparing the polynucleotides of the microbe that are expressed *in vivo* at different stages of infection of the microbe.

12. The method of claim 11 wherein the first expression library and the second expression library are the same expression library.

13. A method of comparing polynucleotides of a microbe that are expressed *in vivo*, wherein the microbe has infected its host by different routes of infection comprising the steps of:
- 5 (a) adsorbing a first sera sample from one or more hosts infected with or previously infected with the microbe, with cells or cellular extracts of the microbe that have been grown *in vitro*, wherein each host has been infected by about the same route of infection;
- 10 (b) adsorbing a second sera sample from one or more hosts infected with or previously infected with the microbe, with cells or cellular extracts of the microbe that have been grown *in vitro*, wherein each host has been infected by about the same route of infection, wherein the route of infection is different from the route of infection in step (a);
- (c) isolating unadsorbed antibodies from the first serum sample and from the second serum sample;
- 15 (d) probing a first expression library of the microbe with the unadsorbed antibodies from the first serum sample, and probing a second expression library with the unadsorbed antibodies from the second serum sample, wherein polynucleotides of the microbe that are expressed *in vivo* are identified for the first and second serum sample; and
- 20 (e) comparing the polynucleotides of the microbe that are expressed *in vivo* by different routes of infection of the microbe.
14. The method of claim 13 wherein the first expression library and the second expression library are the same expression library.

15. A method of confirming an animal model of microbial infection as a valid model comprising the steps of:
- (a) adsorbing a first sera sample from one or more animal model hosts infected with or previously infected with a microbe, with cells or cellular extracts of the microbe that have been grown *in vitro*;
- (b) adsorbing a second sera sample from one or more second hosts infected with or previously infected with the microbe, with cells or cellular extracts of the microbe that have been grown *in vitro*; wherein the second host is a different species of animal than the animal model host;
- (c) isolating unadsorbed antibodies from the first serum sample and from the second serum sample;
- (d) probing a first expression library of the microbe with the unadsorbed antibodies from the first serum sample, and probing a second expression library with the unadsorbed antibodies from the second serum sample, wherein polynucleotides of the microbe that are expressed *in vivo* are identified for the first and second serum sample; and
- (e) comparing the polynucleotides of the microbe that are expressed *in vivo* in the animal model host and the second host;
- wherein if the polynucleotides expressed *in vivo* in the animal model and in the second host are the same or similar, then the animal model is confirmed as a valid model.
16. The method of claim 15 wherein the first expression library and the second expression library are the same expression library.

17. The method of claim 15 wherein the animal model host and the second host are selected from the group consisting of comprise humans, baboons, chimpanzees, macaques, cattle, sheep, pigs, horses, goats, dogs, cats, rabbits, guinea pigs, rats, mice, chickens, ducks, fish, and shellfish.